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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/214,848	01/14/1999	TERUAKI SEKINE	1208/P502PCT	8123

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EXAMINER

CHOI, FRANK I

ART UNIT PAPER NUMBER

1616

DATE MAILED: 09/29/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No. 09/214,848	Applicant(s) SEKINE, TERUAKI	
	Examiner Frank I. Choi	Art Unit 1616	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 5/26/2005, 7/27/2005, 9/12/2005.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 12-27, 31, 32 and 34-39 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 12-27, 31, 32, 34-39 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☒ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. _____.
 3. ☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- * See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|--|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413)
Paper No(s)/Mail Date. _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152) |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)
Paper No(s)/Mail Date _____ | 6) <input type="checkbox"/> Other: _____ |

LD

DETAILED ACTION

A request for continued examination under 37 CFR 1.114 was filed in this application after appeal to the Board of Patent Appeals and Interferences, but prior to a decision on the appeal. Since this application is eligible for continued examination under 37 CFR 1.114 and the fee set forth in 37 CFR 1.17(e) has been timely paid, the appeal has been withdrawn pursuant to 37 CFR 1.114 and prosecution in this application has been reopened pursuant to 37 CFR 1.114. Applicant's submission filed on 5/26/2005 and 9/12/2005 has been entered.

Claim Rejections - 35 USC § 112

35 U.S.C. 101 reads as follows:

Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 12-27, 31,32,34-39 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. Applicant does not cite and Examiner has been unable to determine any disclosure which sets forth the limitation "non-specifically" in relation to activated lymphocytes.

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As such, it appears the inventor's did not have possession of the claimed subject matter at the time the application was filed.

Claims 15-17 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention for the following reasons:

A single claim which claims both a product and the method steps of using the apparatus is indefinite under 35 U.S.C. 112, second paragraph. See *In Ex parte Lyell*, 17 USPQ2d 1548 (Bd. Pat. App. & Inter. 1990) (a claim directed to an automatic transmission workstand and the method steps of using it was held to be ambiguous and properly rejected under 35 U.S.C. 112, second paragraph). In this case, the claims are directed to activated lymphocytes and method of steps of using by administration in a patient. Further, claims 15-17 are also rejected under 35 U.S.C. 101 based on the theory that the claim is directed to neither a "process" nor a "composition of matter," but rather embraces or overlaps two different statutory classes of invention set forth in 35 U.S.C. 101 which is drafted so as to set forth the statutory classes of invention in the alternative only. See *Id.* at 1551. See MPEP Section 2173.05(p)(II).

Claim Rejections - 35 USC § 102/103

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

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(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

Claims 12, 13, 18, 22, 35, 36, 38 are rejected under 35 U.S.C. 102(b) as anticipated by or, in the alternative, under 35 U.S.C. 103(a) as obvious over Santamaria et al.

Santamaria et al. expressly discloses cytomegalovirus primed peripheral blood mononuclear cells from seropositive subjects which are stimulated by anti-CD3 coated onto polystyrene beads plus interleukin-2 falling within the scope of applicant's claims (Abstract).

Alternatively, at the very least the claimed invention is rendered obvious within the meaning of 35 USC 103, because the prior art discloses products and uses that contain the same exact ingredients/components as that of the claimed invention. See *In re Fitzgerald*, 619 F.2d 67, 205 USPQ 594 (CCPA 1980). See also *In re May*, 197 USPQ 601, 607 (CCPA 1978).

Claims 12, 14-18, 23-27, 35, 37 are rejected under 35 U.S.C. 102(b) as anticipated by or, in the alternative, under 35 U.S.C. 103(a) as obvious over Koenig et al.

Koenig et al. expressly discloses compositions comprising autologous lymphocytes from an AIDS patient activated with IL-2 and OKT3 which activated autologous lymphocytes at doses of 28×10^9 , 12×10^9 and 13×10^9 were resuspended in normal saline and human serum albumin and reinfused into the patient for treatment of the patient's HIV infection falling within the scope of applicant's claims (Pg. 334-335).

Alternatively, at the very least the claimed invention is rendered obvious within the meaning of 35 USC 103, because the prior art discloses products and uses that contain the same exact ingredients/components as that of the claimed invention. See *In re Fitzgerald*, 205 USPQ 594 (CCPA 1980). See also *In re May*, 197 USPQ 601, 607 (CCPA 1978). Although, Koenig et

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al. appears to disclose the use of soluble OKT3 instead of solid phase OKT3, the claim is directed to a product not a process. As such, the burden is on Applicant to show that activated lymphocytes using solid OKT3 are different from activated lymphocytes using soluble OKT3.

Claims 12-27, 31, 32, 34-39 are rejected under 35 U.S.C. 103(a) as being unpatentable over Ochoa et al. (U.S. Pat. 5,443,983) in view of Rosenberg (US Pat. 4,690,915), Melder et al., the acknowledged prior art, Wallace et al. or Rooney et al., Babbit et al. (US Pat. 5,766,920), Ochoa et al. (US Pat. 5,296,353), Santamaria et al. and Buseyne et al.

Ochoa et al. (U.S. Pat. 5,443,983) teach a method of developing LAK activity in lymphocytes comprising contacting lymphocytes with IL-2 and an anti-CD3 antibody and a method of administering the same suspended in a phosphate buffered saline supplemented with human serum albumin to an AIDS patient (Column 11, lines 49-68, Column 12, lines 1-50, Claims 1-8).

Rosenberg teaches that lymphocytes activated with IL-2 are effective against cancers, viral and other infective diseases, autoimmune diseases, for the correction immune-deficiency diseases, etc. (Column 4, lines 29-54).

Melder et al. teaches that natural killer (NK) cells have been shown to aid in the control of viral infections by killing virus-infected cells, including cells infected with HIV (pg. 101 1). It is further taught that the lymphokine activated killer (LAK) cells, activated with IL-2, were effective against HIV-infected cells and that the LAK cells which killed HIV-infected target cells were the same as those that kill tumor target cells (pg. 1014). It is taught that a generalized cytotoxic action of NK cells occurs (pg. 1014). It is further taught that cytotoxic lymphocytes are able to recognize cells infected by cytomegalovirus (pg. 1014).

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Applicant acknowledges that T-cells are involved in cellular immunity against cancer and viruses (Specification, Pgs. 1, 2). Further, it is acknowledged that lymphocytes, including T-cells and NK cells, can be activated and stimulated by IL-2 and that lymphocytes can be activated and stimulated with IL-2, with or without CD3 antibodies, including against viruses, such as, EBV and CMV (Specification, pgs. 3,4).

Wallace et al. or Rooney et al. teach that T-cells activated with IL-2 are effective against EBV (See entire disclosure of each).

Babbitt et al. teach activation of autologous T-lymphocytes with OKT3 and cytokines, including IL-2, for treatment of viruses, such as herpesvirus, such as herpes simplex virus and cytomegalovirus, and Epstein Barr virus (See entire document, especially, Column 2, lines 22-68, Column 3, Column 7, lines 40-49, Column 20, lines 53-68, Column 21, lines 1-16). Babbitt discloses solid phase OKT3 but that solution phase is preferred (Column 12, lines 1, 2).

Ochoa et al. (US Pat. 5,296,353) teach activation of autologous T-lymphocytes with anti-CD3, such as OKT3, and cytokines, including IL-2, for treatment of cytomegalovirus and Epstein Barr virus (See entire document, especially, Column 3, lines 32-50, Column 7, lines 54-68, Column 8, lines 1-35, Column 11, lines 29-54, Column 12, lines 15-54).

Santamaria et al. disclose cytomegalovirus primed peripheral blood mononuclear cells from seropositive subjects which are stimulated by anti-CD3 coated onto polystyrene beads plus interleukin-2 and that polystyrene coated with antibodies can induce the long term-growth of antigen specific T-cell lines in the absence of specific antigen and feeder cells, often unavailable (Abstract).

Buseyne et al. disclose that stimulation by anti-CD3 and interleukin-2 is non-specific (Abstract).

The difference between the prior art and the claimed invention is that the prior art does not expressly disclose a method of treating viral infection with a non-specifically activated lymphocytes effective against viral infections obtained by culturing lymphocytes derived from virally infected patients in a culture medium comprising anti-CD3 antibodies in a solid phase and interleukin-2 to proliferate and activate in vitro said lymphocytes which is suspended in phosphate buffered saline and albumin. However, the prior art amply suggests the same as the prior art discloses the activation of autologous lymphocytes which can be used to treat viral infections which lymphocytes are activated by interleukin-2 and anti-CD3, the use of solid phase OTK3, and suspension of lymphocytes activated with interleukin-2 and anti-CD3 which are suspended in phosphate buffered saline and albumin. As such, it would have been well within the skill of and one of ordinary skill in the art would have been motivated to suspend the activated autologous lymphocytes in phosphate buffered saline and albumin with the expectation that the same can be safely administered to a virally infected patient and be effective for treatment of the viral infection.

Applicant's arguments have been duly considered but they are deemed unpersuasive.

In response to applicant's arguments against the references individually, one cannot show nonobviousness by attacking references individually where the rejections are based on combinations of references. See *In re Keller*, 208 USPQ 871 (CCPA 1981); *In re Merck & Co.*, 231 USPQ 375 (Fed. Cir. 1986). Further, the test for obviousness is not whether the features of a secondary reference may be bodily incorporated into the structure of the primary reference; nor is it that the claimed invention must be expressly suggested in any one or all of the references. Rather, the test is what the combined teachings of the references would have suggested to those of ordinary skill in the art. See *In re Keller*, 208 USPQ 871 (CCPA 1981).

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Applicant's chart fails to account for the broader disclosure set forth in the prior art as indicated above which does disclose treatment of virally infected patients with activated autologous lymphocytes using interleukin-2 and OTK3 in the solid phase. A reference may be relied upon for all that it would have reasonably suggested to one having ordinary skill in the art, including nonpreferred embodiments. *Merck & Co. v. Biocraft Laboratories*, 10 USPQ2d 1843 (Fed. Cir.), cert. denied, 493 U.S. 975 (1989). See also *Celeritas Technologies Ltd. v. Rockwell International Corp.*, 47 USPQ2d 1516, 1522-23 (Fed. Cir. 1998) (The court held that the prior art anticipated the claims even though it taught away from the claimed invention. "The fact that a modem with a single carrier data signal is shown to be less than optimal does not vitiate the fact that it is disclosed."). Disclosed examples and preferred embodiments do not constitute a teaching away from a broader disclosure or nonpreferred embodiments. *In re Susi*, 169 USPQ 423 (CCPA 1971). "A known or obvious composition does not become patentable simply because it has been described as somewhat inferior to some other product for the same use." *In re Gurley*, 31 USPQ2d 1130, 1132 (Fed. Cir. 1994) (The invention was directed to an epoxy impregnated fiber-reinforced printed circuit material. The applied prior art reference taught a printed circuit material similar to that of the claims but impregnated with polyester-imide resin instead of epoxy. The reference, however, disclosed that epoxy was known for this use, but that epoxy impregnated circuit boards have "relatively acceptable dimensional stability" and "some degree of flexibility," but are inferior to circuit boards impregnated with polyester-imide resins. The court upheld the rejection concluding that applicant's argument that the reference teaches away from using epoxy was insufficient to overcome the rejection since "Gurley asserted no discovery beyond what was known in the art." 31 USPQ2d at 1132.).

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Applicant has no evidence that the concept of Applicant's claimed invention did not appear prior to Shimizu et al. or Applicant's effective filing date. In any case, said argument goes to novelty and anticipation not obviousness. As indicated above, Applicant's discussion of example 1 of Ochoa ('353) and Rooney et al. and Wallace et al. does not overcome the rejection as the rejection is based on a combination of references. Obviousness does not require absolute predictability. Applicant provides no evidence that effect in Example 1 of Ochoa was not caused by the activated lymphocyte. In re Schulze, 145 USPQ 716, 718 (CCPA 1965); In re Geisler, 43 USPQ2d 1362 (Fed. Cir. 1997) ("An assertion of what seems to follow from common experience is just attorney argument and not the kind of factual evidence that is required to rebut a prima facie case of obviousness."). Since Applicant's Specification does not disclose "non-specifically" activated T-cells, and, thus, does not define what was intended by said limitation, it cannot be concluded that that activated lymphocytes in Rooney et al. and Wallace et al. are not non-specifically activated T-cells. In any case, the rejection is based on a combination of references which disclose the use of interleukin-2 and OTK3, as such, since the same activators are used and activation by the same is non-specific, it appears that the limitations of the claims are met.

As such, as indicated above, there is motivation to combine and/or modify the references and the disclosures while also disclosing preferred embodiments or examples which are not the same as the claimed invention, the same do not constitute a teaching away from the claimed invention.

Therefore, the claimed invention, as a whole, would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made, because every element of the invention has been collectively taught by the combined teachings of the references.

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Conclusion

A facsimile center has been established in Technology Center 1600. The hours of operation are Monday through Friday, 8:45 AM to 4:45 PM. The telecopier number for accessing the facsimile machine is 571-273-8300.


Any inquiry concerning this communication or earlier communications from the examiner should be directed to Frank Choi whose telephone number is (571)272-0610. Examiner maintains a flexible schedule. However, Examiner may generally be reached Monday-Friday, 8:00 am – 5:30 pm (EST), except the first Friday of the each biweek which is Examiner's normally scheduled day off.

If attempts to reach the Examiner by telephone are unsuccessful, the Examiner's Supervisor, Mr. Gary Kunz, can be reached at 571-272-0887. Additionally, Technology Center 1600's Receptionist and Customer Service can be reached at (571) 272-1600.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

FIC

September 23, 2005



JOHN PAK
PRIMARY EXAMINER
GROUP 1600